

**REMARKS****Formalities**

Claims 10-13 and 24-51 are pending in the application. Claims 28-46 were allowed. Claims 10-13, 24-27 and 48-51 have been canceled, including claims 10-13 and 24-27, which were withdrawn from consideration as being drawn to a non-elected invention. Claim 47 has been amended. The amendments to the claims do not add or constitute new matter. Support for the amendments may be found throughout the specification and originally filed claims. More particularly, support for the amendment to claim 47 may be found, for example, at page 12, line 1 through page 13, line 5, of the specification.

The foregoing amendments are made solely to expedite prosecution of the instant application and properly respond to the final rejection, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 28-47 are pending in the instant application.

**Rejections*****Rejection under 35 U.S.C. § 112, second paragraph***

The Examiner rejected claims 47 and 48 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicant respectfully traverses this rejection.

Specifically, the Examiner asserts that claims 47 and 48 are incomplete for omitting essential steps, such omission amounting to a gap between the steps. The Examiner alleges that this omitted step is selecting for the ES cells that have undergone homologous recombination. The Applicant disagrees that the omission of this step amounts to a gap between steps, and submits that the steps recited in the previous version of the claim point out the steps regarded as the invention. The Examiner has further alleged that the phrase “wherein the pseudopregnant mouse gives birth” renders the claim indefinite because a pseudopregnant mouse cannot give birth. Applicants also traverse this aspect of the rejection. Although Applicants disagree with the Examiner’s conclusions and traverse the rejection, claim 47 has been amended to include the

allegedly omitted step and recite that the “resultant mouse” and not a pseudopregnant mouse gives birth. Claim 48 has been canceled. Therefore, the rejection is no longer relevant, and Applicant respectfully requests withdrawal of the rejection.

Applicant submits that the pending claims are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

***Rejection under 35 U.S.C. § 103***

Claims 49-51 were rejected by the Examiner as being unpatentable under 35 U.S.C. § 103(a) based upon the teachings of Mansour *et al.*, 1988, *Nature* 336(24):348-352 (“Mansour”), in view of Sawada *et al.*, 1994, *Biochem Biophys Res Comm* 203(1):479-484 (“Sawada”) and further in view of Ogata *et al.*, 1999, *J. Biol Chem.* 274(18):12905-12909 (“Ogata”). Applicant respectfully traverses this rejection.

Mansour describes a general approach for isolating embryonic stem cells containing a targeted mutation in a gene, provided that a cloned fragment of the gene is available. Specifically, Mansour teaches the targeted disruption of the *hprt* gene and the proto-oncogene *int-2* in mouse embryo-derived stem cells by homologous recombination using targeting constructs pRV9.1/TK and pINT-2-N/TK, respectively. The Examiner concedes, however, that Mansour does not teach how to make a PTP36 targeting construct.

According to the Examiner, Sawada discloses the cloning and characterization of a novel non-receptor protein tyrosine phosphatase (PTP36) from murine thymus. Sawada provide the nucleic acid sequence encoding PTP36.

Ogata relates to overexpression of PTP36 in HeLa cells and the effect of the overexpression on cell adhesion, cell growth and cytoskeletons. Ogada disclose that induction of PTP36 overexpression in HeLa cells resulted in cells to spread less well, grow more slowly and adhere to the extracellular matrix proteins less well than in uninduced cells, and further disclosed decreases in the actin stress fibers and number of focal adhesions in these cells. Ogada suggests a role for PTP36 in the regulation of these processes.

As a basis of the obviousness rejection under 35 U.S.C. § 103, the Examiner asserts that the ordinary artisan would have been motivated to make a PTP36 knockout construct in order to study the precise role PTP36 plays in the regulation of cell growth, adhesion and cytoskeleton. The Examiner further asserts that the ordinary artisan would have had a reasonable expectation

of success because of the teachings of Mansour, Sawada and Ogata in light of the high level of skill in the art of making gene targeting constructs and ES cells comprising the constructs as claimed. The Examiner has stated that the recitation of the phenotype in the transgenic mice observed by Applicant as a result of disruption using the claimed targeting construct does not carry patentable weight as it is only the intended use of the targeting construct. The Applicant respectfully disagrees. The Applicant submits that the phenotypic properties resulting from disruption using the claimed targeting construct show that the construct does possess properties that distinguish the targeting construct from the subject matter described in the prior art references. However, as the rejection has been made final, Applicant has canceled claims 49-51 to overcome the rejection.

As the rejection under 35 U.S.C. § 103 is no longer relevant, and claims 28-47 are not obvious in view of the sole or combined teachings of Mansour, Sawada and/or Ogata, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 103.

**Claim Objections**

Claim 48 has been objected to by the Examiner under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 28. The Applicant disagrees. However, Applicant has overcome the objection by the cancellation of claim 28.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-758.

Respectfully submitted,

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